

**REMARKS/ARGUMENTS**

With this amendment, Claims 1-20 and 25-30 are pending. Claims 21-24 are cancelled without prejudice to subsequent revival. An IDS is also submitted for the Examiner's consideration.

**I. Status of the claims**

Claims 21-24 are cancelled without prejudice to subsequent revival.

Claims 1, 12, 18, and 25 are amended to recite induces apoptosis, rather than affects apoptosis. Support for this amendment is found throughout the application, for example at Example 6, page 46 and Figure 9. This amendment adds no new matter.

New claims 27 and 28 are added and depend from claim 1. The new claims recite either 90 or 95% identity to an Apop3 nucleic acid sequence. Support for this amendment is found throughout the specification, *e.g.*, at page 13, lines 3-6. This amendment adds no new matter.

New claims 29 and 30 are added and depend from claim 12. The new claims recite either 90 or 95% identity to an Apop3 polypeptide sequence. Support for this amendment is found throughout the specification, *e.g.*, at page 5, lines 22-25. This amendment adds no new matter.

**II. Rejection under 35 U.S.C. §112, first paragraph, enablement**

Claims 1, 3, 4, 6-12, 25, and 26 are rejected under 35 U.S.C. §112, first paragraph because the specification allegedly fails to provide enablement for the claimed invention. The Examiner at page 3 of the Office Action indicates that the rejection would be obviated by amending the claims to read "inducing" apoptosis. In order to expedite prosecution, claims 1, 12, 18, and 25 are amended to recite the Apop3 protein induces apoptosis, rather than affects apoptosis.

The Advisory Action also states that, although the specification enables claims reciting SEQ ID NO:5 and SEQ ID NO:6, the full scope of the claims, *e.g.*, 85% identity to SEQ

ID NO:5 or to SEQ ID NO:6, is not enabled. To the extent the rejection applies to the amended claims, Applicants respectfully traverse the rejection.

The Examiner appears to have focused improperly on inoperative embodiments, leading to the conclusion that undue experimentation would be required to identify biologically active enzymes and their encoding nucleic acids of the claimed invention. However, the proper test of enablement is “whether one skilled in the art could make or use the claimed invention from the disclosure in the patent coupled with information known in the art without undue experimentation” (*see, e.g.*, MPEP §2164.01). In the present application, one of skill would know how to avoid inoperative embodiments and make biologically active polypeptides and the nucleic acids that encode them, without undue experimentation (*see, In re Cook and Merigold*, 169 USPQ 299, 301 (C.C.P.A. 1971)). Moreover, the present application provides guidance in the form of assays and working examples for identification of active Apop3 polypeptides.

Claims reading on inoperative embodiments are enabled if the skilled artisan understands how to avoid inoperative embodiments. As described by the court in *In re Cook and Merigold*, 169 USPQ 302:

Many patented claims read on vast numbers of inoperative embodiments in the trivial sense that they can and do omit ‘factors which must be presumed to be within the level of ordinary skill in the art’... There is nothing wrong with this so long as it would be obvious to one of ordinary skill in the relevant art how to include those factors in such a manner as to make the embodiment operative rather than inoperative.

*See, In re Cook and Merigold*, 169 USPQ at 302 (quoting in part *In re Skrivan*, 166 USPQ 85, 88 (C.C.P.A. 1970)).

The claims are directed to Apop3 polypeptides that induce apoptosis and that comprise an amino acid or nucleic acid sequence with at least 80% identity to a reference sequence, *i.e.*, SEQ ID NO:5 or SEQ ID NO:6. Also included are claims that are directed to nucleic acids of SEQ ID NO:5, *i.e.*, claims 2 and 7; claims that are directed to nucleic acids that encode SEQ ID NO:6, *i.e.*, claim 5; claims that are directed to a polypeptide of SEQ ID NO:6, *i.e.*, claims 13 and 18; and claims that are directed to polypeptides encoded by a nucleic acid comprising SEQ ID NO:5, *i.e.*, claim 14. New claims 27-30 are directed to Apop3 nucleic acids

that comprise sequences at least 90 or 95% identical to SEQ ID NO:5 and to Apop3 polypeptides that comprise sequences at least 90 or 95% identical to SEQ ID NO:6.

The Examiner appears concerned that if one of skill in the art choose to change the amino acid sequence of the Apop3 protein, the skilled artisan would likely choose to make an inoperative embodiment. The Examiner's concern is misplaced because those of skill in the art will be able to identify conserved amino acids within those sequences and will know to avoid detrimental changes to those amino acids. The properties of amino acids are well known to those of skill in the art. Amino acids are characterized by their hydrophobicity, charge, and bulk of side chains, for example. Knowing the properties of particular amino acids, the skilled artisan could easily choose appropriate amino acids to change in an Apop3 protein and could avoid adding amino acids that would be detrimental to the structure or function of the polypeptide. In addition, those of skill in the art are aware of methods, like alanine scanning, where amino acid sequences are manipulated with minimal disruption of protein structure or function.

Factors such as the amount of guidance presented in the specification and the presence of working examples must be considered to determine whether undue experimentation is required to practice the claimed invention (*see, Ex Parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int. 1985) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988)). As described in *Wands*, "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed" (*see, Wands*, USPQ2d at 1404, quoting *In re Jackson*, 217 USPQ 804 (Bd. Pat. App. & Int. 1982)).

The specification also provides standard assays and working examples for identifying Apo3 proteins and nucleic acids and for assaying apoptosis. (See, e.g., specification at page 32, line 27 through page 34, line 4 and Examples 6 and 7 on pages 44-45.) The exemplified assays were performed on wild type and mutated Apop3 proteins and clearly demonstrate their use for identifying Apop3 proteins that induce apoptosis. Identification of biologically active Apop3 proteins is, therefore, well within the means of one of skill of the art, without undue experimentation.

Applicants also respectfully bring to the Examiner's attention, that, at a minimum, claims 2, 5, 7, 13, 14 and 18 are enabled according to the Advisory Action and are thus allowable.

In view of the above amendments and remarks, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112, first paragraph, for alleged lack of enablement.

**CONCLUSION**

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

  
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